

## Format for ANSWERING REVIEWERS

March 26, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript NO: 25239-edited.doc).

**Title:** Subclinical hypothyroidism in atopic South Italian children

**Authors:** Marcella Pedullà, Vincenzo Fierro, Pierluigi Marzuillo, Ester Del Tufo, Anna Grandone, Laura Perrone, and Emanuele Miraglia del Giudice.

**Name of Journal:** *World Journal of Clinical Pediatrics*

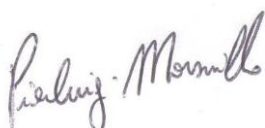
**ESPS Manuscript NO:** 25239

The manuscript has been improved according to the suggestions of reviewers:

- (1) we accepted all the suggestion of the Reviewers presented in word track changes mode
- (2) we critically revised the written English to improve the fluidity of the text
- (3) we modified the figure legend of figure 1

We hope that our manuscript will be of interest for the readers of the *World Journal of Clinical Pediatrics*.

Sincerely yours,



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**Reviewer 00742006**

**Comments: Accept**

*Answer: thank you*

**Reviewer 02565607**

**Comments:** The association among obesity, chronic inflammation and subclinical hypothyroidism (SCH) is a very interesting topic. The authors tried to address that atopy could be associated with SCH possibly via atopic inflammation. The authors did find a significant higher prevalence of SCH in the groups with average or higher CRP level compared to that with lower CRP level. And this seemed to be the only data based on which the authors drew that conclusion that there is an association between SCH and atopy, while it's hard to confirm this association without adjusting for the potential confounders. Just as what the authors reviewed in the manuscript, obesity is associated with SCH, and some studies found that obesity is associated with atopy possibly because of the chronic inflammation status. So obviously, obesity is one of the potential confounders. And in line 147, the authors mentioned the criteria they applied to diagnose SCH in their study. While anti-thyroid antibodies value in the normal range should not be one of the criteria in the diagnosis of SCH. Since the definition of SCH in children varies in different studies, I also hope to see the authors' more detail explain why they applied a cut-off point of TSH over 5 mUI/mL in their study. In addition, there are needs to better present the data in Figure 1, e.g. put Complement C3 levels values according to low grade inflammation in both atopic and not atopic as Figure 1 (a) and total IgE serum values according to low grade inflammation in both atopic and not atopic as Figure 1 (b). If it is possible, put the statistic analyses into the figure, e.g. the statistic analyses on the basis of the CRP serum levels as shown in Table 2 as well as statistic analyses between atopic and not atopic.

*Answer: thank you for your comments. We agree with you that anti-thyroid antibodies should not be one of the criteria in the diagnosis of SCH. We evaluated the anti-thyroid antibodies to exclude the thyroiditis from the SCH population with the aim to have a well-selected population without the presence of anti-thyroid autoimmunity. We applied as cut-off point of SCH a TSH> 5 mUI/mL because it was the cut off identified by the "European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children" (we added this information in the text in the material and methods section, see lines 147-149 of the new version of the manuscript). As*

*required, we added the low grade inflammation cut-offs and the statistic analyses on the basis of the CRP serum levels in the figure 1 legend (see lines 331-338 of the new version of the manuscript). We added the Group 1, Group 2 and Group 3 also in the figure 1.*

**Reviewer 00503773**

**Comments:** I read the manuscript named "Subclinical hypothyroidism in atopic South Italian children " that have been submitted to the World Journal of Clinical Pediatrics. (ESPS Manuscript NO: 25239) and my recommendations are as follows. Title: It is accurately reflects the major topic and contents of the study. Abstract: Adequate, summarizing the topic. Discussion: Adequate References are appropriate, relevant, and updated. Tables and figures are reflects the major findings of the study, and they are appropriately presented. This study is clearly presented . This manuscript gives additional new knowledge to the literature. I think that this manuscript is suitable and worth to be published in the World Journal of Clinical Pediatrics.

*Answer: thank you.*